

What is claimed is:

1. A polypeptide comprising the amino acid sequence YDIXYYXXE, wherein X is any synthetic or naturally occurring amino acid residue, such that the polypeptide binds HIV gp120 under physiological conditions, and wherein said polypeptide comprises less than about 100 contiguous amino acids that are identical to or substantially identical to the amino acid sequence of the human CCR5 chemokine receptor.

2. The polypeptide of claim 1, which comprises less than about 50 contiguous amino acids that are identical to or substantially identical to the amino acid sequence of the human CCR5 chemokine receptor.

3. The polypeptide of claim 2, which comprises less than about 25 contiguous amino acids that are identical to or substantially identical to the amino acid sequence of the human CCR5 chemokine receptor.

4. The polypeptide of claim 3, which comprises less than about 13 amino acids that are identical to or substantially identical to the amino acid sequence of the human CCR5 chemokine receptor.

5. The polypeptide of claim 4, which consists essentially of YDIXYYXXE.

30 6. The polypeptide of any of claims 1-5, which comprises the amino acid sequence YDIN*YYT*S*E, wherein

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~~N* is asparaginyl or a synthetic or naturally occurring substitute therefor, T* is threoninyl or a synthetic or naturally occurring substitute therefor, and S* is serinyl or a synthetic or naturally occurring substitute therefor.~~

7. The polypeptide of claim 6, wherein N* is asparaginyl, T* is threoninyl, and S* is serinyl.

~~10 8. The polypeptide of any of claims 1-6, comprising the amino acid sequence M*D*YQ*V*S*SP*IYDIN*YYT*S*E, wherein each letter indicates the standard amino acid residue designated by that letter, and a letter followed directly by an * indicates that any synthetic or naturally occurring amino acid can occupy that position.~~

~~9. The polypeptide of claim 8, wherein said letter followed directly by an * indicates the amino acid residue represented by the letter or a synthetic or naturally occurring conservative or neutral amino acid substitution therefor.~~

10. The polypeptide of claim 9, wherein said amino acid sequence is MDYQVSSPIYDINYTSE.

11. A polypeptide comprising the amino acid sequence XEXIXIYXXXNYXXX, wherein X is any synthetic or naturally occurring amino acid, such that the polypeptide binds HIV gp120 under physiological conditions, and wherein said polypeptide less than about 100 contiguous

amino acids that are identical to or substantially identical to the amino acid sequence of the human CXCR4 chemokine receptor.

5 12. The polypeptide of claim 11, which comprises less than about 50 contiguous amino acids that are identical to or substantially identical to the amino acid sequence of the human CXCR4 chemokine receptor.

10 13. The polypeptide of claim 11, which comprises less than 25 contiguous amino acids that are identical to or substantially identical to the amino acid sequence of the human CXCR4 chemokine receptor.

15 14. The polypeptide of claim 13, which consists essentially of EXIXIYXXXNY.

15. The polypeptide of any of claims 11-14, which comprises the amino acid sequence
~~M*EG*IS*IYT*S*D*NYT*E*E*~~, wherein each letter indicates the standard amino acid residue designated by that letter, and each letter followed directly by an * indicates the amino acid residue represented by the letter or a synthetic or naturally occurring conservative or neutral amino acid substitution therefor.

16. The polypeptide of claim 15, wherein said amino acid sequence M*EG*IS*IYT*S*D*NYT*E*E* is
M*EGISIYTSNDNYT*E*E*.

17. A polypeptide comprising the amino acid sequence EHQAFLQFS, such that the polypeptide binds with HIV gp120 under physiological conditions and wherein said polypeptide comprises less than about 100 contiguous 5 amino acids that are identical to or substantially identical to the amino acid sequence of the human STRL33 chemokine receptor.

18. The polypeptide of claim 17, which comprises 10 less than about 50 contiguous amino acid that are identical to or substantially identical to the amino acid sequence of the human STRL33 chemokine receptor.

19. The polypeptide of claim 18, which comprises 15 less than about 25 contiguous amino acids that are identical to or substantially identical to the amino acid sequence of the human STRL33 chemokine receptor.

20. The polypeptide of claim 19, which consists 20 essentially of the sequence EHQAFLQFS.

21. A polypeptide comprising at least a portion or all of an amino acid sequence selected from the group consisting of LPPLYSLVFIFGFVGNML, QWDFGNTMCQLLTGLYFIGFFS, SQYQFWKNFQTLKIVILG, APYNIVLLLNTFQEFFGLNNCS, and YAFVGEKFRNYLLVFFQK, wherein the polypeptide binds with HIV gp120 under physiological conditions and comprises less than about 100 amino acid residues that are identical to or substantially identical to the amino acid 30 sequence of the human CCR5 chemokine receptor.

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22. A polypeptide comprising at least a portion or all of an amino acid sequence selected from the group consisting of LLLTIPDFIFANVSEADD (165-182), VVFQFQHIMVGLILPGIV (197-214), and IDSFILEIIKQGCEFEN (261-278), wherein the polypeptide binds with HIV gp120 under physiological conditions and comprises less than about 100 amino acid residues that are identical to or substantially identical to the amino acid sequence of the human CXCR4 chemokine receptor.
- 10 23. A polypeptide comprising at least a portion or all of an amino acid sequence selected from the group consisting of LVISIFYHKLQLSLTDVFL (53-70), PFWAYAGIHEWVFGQVMC (85-102), EAISTVVLATQM TLGF (185-202), LTMIVCVSIIKTLHAG (205-222), MAVFLLTQMPFNLMKFIRSTHW (237-258), HWEYYAMTSFHYTIMVTE (257-274), ACLNPVLYAFVSLKFRKN (281-298) and SKTFSASHNVEATSMFQL (325-342), wherein the polypeptide binds with HIV gp120 under physiological conditions and comprises less than about 100 amino acid residues that are identical to or substantially identical to the amino acid sequence of the human STRL33 chemokine receptor.
- 25 24. A polypeptide comprising at least a portion of or all of an amino acid sequence selected from the group consisting of DTYICEVED, EEVQLLVFGLTANS, THLLQGQSLTLTLES, and GEQVEFSFPLAFTVE, wherein the polypeptide binds with HIV gp120 under physiological conditions and wherein the polypeptide comprises less than about 100 amino acids that are identical to or

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~~substantially identical to the amino acid sequence of the human CD4 cell-surface protein.~~

25. A polypeptide of any of claims 21-24, which
5 comprises all of the amino acid sequence and 0 to about 6
conservative or neutral amino acid substitutions.

26. The polypeptide of claim 25, comprising 0 amino
acid substitutions.

10 27. The polypeptide of any of claims 21-26, which
comprises less than about 50 amino acids that are
identical to or substantially identical to a protein that
naturally has the amino acid sequence.

15 28. The polypeptide of any of claims 21-26, which
comprises less than about 25 amino acids that are
identical to or substantially identical to a protein that
naturally has the amino acid sequence.

20 29. The polypeptide of any of claims 1-28, wherein
said polypeptide further comprises a pharmaceutically
acceptable substituent.

25 30. A composition comprising the polypeptide of any
of claims 1-28, and a carrier.

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31. A nucleic acid encoding the polypeptide of any
of claims 1-28, wherein said nucleic acid can be
30 expressed in a cell.

32. The nucleic acid of claim 31, further comprising a nucleic acid sequence that encodes a signal sequence, wherein said signal sequence is translated as a fusion protein with the polypeptide to form a signal sequence-polypeptide fusion, and wherein said signal sequence can cause secretion of at least the polypeptide out of a cell in which the nucleic acid is expressed.

33. A vector comprising the nucleic acid of claim
10 31 or 32.

34. A method of making an antibody, which method comprises administering an immunogenic amount of a polypeptide of any of claims 1-28 or a nucleic acid of
15 any of claims 31 or 33 to an animal.

35. A method of prophylactically or therapeutically treating HIV infection in a mammal in need thereof, which method comprises administering to said mammal an effective amount of a polypeptide of any of claims 1-28,
20 a nucleic acid of any of claims 31-33, or an anti-antibody to a polypeptide of any of claims 1-28.

36. A method of making an antibody that binds to a gp120 envelope protein of a human immunodeficiency virus-1 (HIV-1), said method comprising:

(a) labeling a polypeptide of any of claims 1-28 to obtain a labeled compound,
30 (b) providing a library of synthetic peptides, wherein said library consists of a multiplicity of synthetically-produced polypeptides that are homologous

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- to a continuous region of an HIV-1 gp120 envelope protein, wherein each polypeptide of said library is substantially isolated from every other polypeptide of said library and is located in a known position,
- 5 (c) individually contacting each polypeptide with said labeled compound such that a portion of the labeled compound can bind with the polypeptide, thereby producing a bound population of each polypeptide and an unbound population of each polypeptide,
- 10 (d) removing substantially all of the unbound labeled compound from the position occupied by each polypeptide,
- 15 (e) measuring the amount of labeled compound that remains co-localized with each polypeptide, to determine the quantity of labeled compound bound by each polypeptide,
- 20 (f) evaluating the amount of labeled compound bound by each polypeptide to identify a portion of the HIV-1 gp120 envelope protein that binds to an (HIV-1)-receptor selected from the group consisting of CCR5, CXCR4, STRL33, and CD4,
- 25 (g) providing an immunizing compound comprising a polypeptide comprising an amino acid sequence that is homologous to said portion of the HIV-1 gp120 envelope protein,
- 30 (h) inserting an immunogenic quantity of said immunizing compound into an animal to cause said animal to produce an antibody that binds with said portion of the HIV-1 gp120 envelope protein.

37. The method of claim 36, wherein said labeled compound comprises a moiety selected from the group consisting of a radioactive atom, an enzyme, a polyhistidinyl moiety, and an antigen that is 5 specifically recognized by a standard antibody.

38. The method of claim 36 or 37, wherein said library consists of a multiplicity of synthetically-produced polypeptides that are identical to a continuous 10 region of an HIV-1 gp120 envelope protein.

39. The method of any of claims 36-38, wherein said polypeptides contain at least about 6 amino acid residues and no more than about 45 amino acid residues.

15 40. The method of claim 39, wherein said polypeptides contain no more than about 30 amino acid residues.

20 41. The method of any of claims 36-40, wherein said library comprises a multiplicity of polypeptides of identical lengths.

42. The method of any of claims 36-41, wherein said 25 library comprises a multiplicity of polypeptides that are homologous to a region of the HIV-1 gp120 envelope protein and have an offset of n amino acid residues, wherein n is an integer of at least 1 and is not greater than the product of length of the longest polypeptide 30 measured in amino acid residues and 1.5.

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43. The method of claim 42, wherein said offset is not greater than the product of length of the longest polypeptide measured in amino acid residues and 1.0.

5 44. The method of claim 42, wherein said offset is not greater than the product of length of the longest polypeptide measured in amino acid residues and 0.5.

10 45. The method of claim 42, wherein said offset is not greater than 30.

46. The method of claim 42, wherein said offset is not greater than 15.

15 47. The method of claim 42, wherein said offset is not greater than 4.

48. The method of any of claims 36-47, wherein each polypeptide is bound to a solid support and is located in 20 a vessel that enables each polypeptide to be covered in a liquid that does not contact any other oligonucleotide of the library.

49. The method of claim 48, wherein each 25 polypeptide is bound to a bead in a vessel or is bound to the well of a multi-well assay plate.

50. The method of claim 36, wherein said step of removing substantially all of the unbound labeled 30 compound comprises the additional steps of (i) removing a liquid containing said unbound labeled compound from a

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solid substrate to which an polypeptide of the library is bound, (ii) applying a quantity of wash-liquid to said solid substrate that is sufficient to cover any portion of said solid substrate or a vessel containing said solid 5 substrate that has been contacted by said labeled compound, and (iii) removing said wash-liquid.

51. The method of any of claims 36-50, wherein said immunizing compound comprises an adjuvant or wherein said 10 polypeptide comprising an amino acid sequence that is homologous to said portion of the HIV gp120 envelope protein is conjugated to a known immunogen.

52. The method of any of claims 36-51, wherein said 15 method is performed in a mammal belonging to a group selected from the group consisting of rodents, canines, felines, and ruminants.

53. The immunizing compound of step (g) of the 20 method of any of claims 36-52.

54. An antibody produced by the method of any of claims 36-53.

25 55. A method of removing HIV from a bodily fluid of a mammal, which method comprises extra-corporeally contacting said bodily fluid with a solid support to which is attached a polypeptide of any of claims 1-28 or an anti-antibody to a polypeptide of any of claims 1-78, 30 or the antibody of claim 54.

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